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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,876	10/19/2001	Steven M. Ruben	PZ001G67AP1D1	8845

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/981,876	RUBEN ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-74 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-74 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 10/19/01.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-74 are pending and under examination as they read on an antibody that specifically binds the SEQ ID NO: 200. Because Depsoit 97904 contains multiple different clone and the ambiguity as which polypeptide the antibody would bind, the Examination of claims 38-74 are examined to the extent of SEQ ID NO: 200 only.

2. Applicant's IDS, filed 10/19/01, is acknowledged, however, references Ab-AE and AM-AN were crossed out as the entire documents were not found. Applicant is invited to produce such documents.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 3-7, 10-11, 19-20, 26-30, 33-34, 38-74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The "portion thereof" which is a monoclonal antibody in claims 3, 26, 40 and 63 is ambiguous and indefinite because only antibody can be a monoclonal antibody and not an antibody portion. It is suggested that the claims be amended to recite, for example "The antibody or portion thereof of claim 1, wherein the antibody is a polyclonal antibody" (claim 3).

B. The "portion thereof" which is a polyclonal antibody in claims 4, 27, 41 and 64 is ambiguous and indefinite because only antibody can be a polyclonal antibody and not an antibody fragment. It is suggested that the claims be amended to recite, for example "The antibody or portion thereof of claim 1, wherein the antibody is a polyclonal antibody" (claim 4).

C. The "portion thereof" which is a chimeric antibody in claims 5, 28, 42 and 65 is ambiguous and indefinite because only antibody can be a chimeric antibody and not an antibody portion. It is suggested that the claims be amended to recite, for example "The antibody or portion thereof of claim 1, wherein the antibody is a chimeric antibody" (claim 4).

D. The "portion thereof" which is a humanized antibody in claims 6, 29, 43 and 66 is ambiguous and indefinite because only antibody can be a humanized antibody and not an antibody portion. It is suggested that the claims be amended to recite, for example "The

antibody or portion thereof of claim 1, wherein the antibody is a monoclonal antibody" (claim 6).

E. The "portion thereof" which is a human antibody in claims 7, 30, 44 and 67 is ambiguous and indefinite because only intact antibody can be a human antibody and not an antibody portion. It is suggested that said claims be amended to recite, for example "The antibody or portion thereof of claim 1, wherein the antibody is a human antibody" (claim 7).

F. Claims 10, 19, 33, 47, 56 and 70 have no antecedent basis in base claims 1, 15, 24, 38, 52 and 61, respectively, because claims 1, 24 recite antibody or fragment thereof per se, whereas a labeled antibody or fragment thereof is recited in claims 10. It is suggested that claim 10, for example, be changed to "A labeled antibody or portion thereof, wherein the antibody or fragment thereof of claim (1) is labeled" and dependent claims thereof be changed to "The labeled antibody or fragment thereof of claim ...".

G. Claims 38, 52 and 61 are indefinite in the recitation "polypeptide encoded by the cDNA contained in ATCC Deposit Number 97904" because ATCC Deposit No. 97904 contain multiple different clones encoding multiple polypeptide and it unclear to which polypeptide the antibody is directed to.

5. 35 U.S.C. § 101 reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

6. Claims 1-74 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility.

Applicants are directed to the Final Utility Guidelines, Federal Register, and Published Friday January 5, 2001.

The instant application has provided a description of an isolated polypeptide and an antibody against the polypeptide. The instant application does not disclose the biological role of the polypeptide or its significance. The instant specification asserts specific utilities for the claimed invention that the polynucleotides or polypeptides are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but not limited to, Hodgkin's Lymphoma, Common Variable Immunodeficiency, and/or other B-cell lymphomas (on pages 97, paragraphs 382-387 in particular). The specification further discloses that polypeptides and polynucleotides corresponding to gene No. 67 (encodes SEQ ID NO: 200 (see Table 1, page 119, 2nd row, in particular) are useful for therapeutic and/or diagnostic purposes, targeting Hodgkin's Lymphoma, B-cell lymphomas, Common Variable Immunodeficiency, or other immune disorders (page 98, paragraph 385, in particular). Further, the specification asserts that

antibodies which specifically binds polypeptide are useful in providing immunolgical probes for differential identification of the tissue(s) or cell type(s) (see page 98, under paragraph 384).

These utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for SEQ ID NO: 200 or antibodies directed to SEQ ID NO: 200. The disclosed polypeptide is said to have a potential function based upon its amino acid sequence homology to 8hs20 protein precursor [*mus musculus*] (see page 97, paragraph 382, and page 98, paragraph 385, in particular). The deduced 123-amino acid expressed primarily in human-B-cells and to a lesser extent in Hodgkin's Lymphoma shares 67% sequence identity with mouse Vpreb3, 43% identity wit a V-lambda segment, and 40% identity with human VPREB. After further research, specific and substantial credible utility might be found for the claimed isolated polypeptide or the antibody directed to the polypeptide. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The presence of a polynucleotide encoding polypeptide of SEQ ID NO: 200 in pre-B cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the polypeptide, which is the claimed antibody binds to, and the disease. Further, in Rosnet et al in Cytogenet cell genet 87:205-208 (199) teaches that the precise function of VPREB3 (SEQ ID NO:200, which claimed antibody binds) is not known (see page 1, 2nd col., line 7).

The instant situation is directly analogous to that which was addressed in *Brenner V. Manson*, 148 U.S. P. Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S. C. § 101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The instant claims are drawn to a polypeptide of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that antibodies directed to SEQ ID NO: 200 are useful in therapeutic and/or diagnostic purposes, targeting Hodgkin's Lymphoma, B-cell lymphomas, Common Variable Immunodeficiency, or other immune disorders, as of the filling date. Until some actual and specific significance can be attributed to the protein identified in the specification as SEQ ID NO: 200 and antibodies against SEQ ID NO:200, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

No single effect of the disclosed Gene No:67 encoding SEQ ID NO: 200, is ascribed to the polypeptide and hence to the antibodies against those polypeptide. Note that while the specification produces the full-length protein recombinantly, no biological activity is established for the full length protein or any of the claimed fragments thereof. As such, further research would be required to identify or research such as studying the properties of the claimed product

itself or the mechanisms in which the material is involved would be required. Since the instant specification does not disclose a credible "real world" use for SEQ ID NO: 200 and the claimed antibodies against SEQ ID NO:200, then the claimed invention as disclosed does not meet the requirements of 35 U.S. C. § 101 as being useful.

The proteins of the instant invention are compounds, which share some structural similarity with 8hs20 protein based on sequence similarity. It is not clear if the polypeptide of the instant application would have the same function in therapeutic and/or diagnostic purposes, targeting Hodgkin's Lymphoma, B-cell lymphomas, Common Variable Immunodeficiency, or other immune disorders as stated at page 98, paragraph 385 of the specification. Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). To employ a protein of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility which, alone, does not support patentablility. Since the instant specification does not disclose a credible "real world" use for the antibodies directed to SEQ ID NO: 200, then the claimed invention as disclosed does not meet the requirement of 35 U.S.C. § 101 as being useful.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-74 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

9. Further, the polypeptide encoded by the cDNA contained in ATCC deposit Number 97904 recited in claims 38, 52 and 61 are essential to the claimed invention. The reproduction of the polypeptide from the disclosed deposit No. 97904 is an extremely unpredictable event because it is known that bacteria contain multiple different clones with the same antibiotic resistant would lead to selective pressure favoring some clones over others and there is no guarantee that the

cDNA encoding the polypeptide of SEQ ID NO: 200 is going to be selected over time. The vector, Uni-XAP XR comprising the cDNA encoding the polypeptide of SEQ ID NO: 200, disclosed in table 1, page 119, 2nd row of the specification, must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The instant specification does not disclose a repeatable process to obtain the vector, and it is not apparent if the vector is readily available to the public.

If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the vector has been deposited under the Budapest Treaty and that the vector will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample *or for the enforceable life of the patent whichever is longer*. See 37 CFR 1.806. If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

If the deposit was made after the effective filing date of the application for a patent in the United States, a verified statement is required from a person in a position to corroborate that the vector described in the specification as filed are the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

10. Furthermore, besides an isolated polypeptide comprising SEQ ID NO: 200 and the amino acid 25-123 of SEQ ID NO: 200 the specification fails to provide any guidance as to how to make an isolated antibody produce by immunizing an animal with any protein whose sequence "comprises" amino acid residues 25-123 of SEQ ID NO:200 in claim 15, or any isolated antibody or portion thereof that specifically binds to a protein whose sequence consists of the amino acid sequence of the secreted polypeptide encoded by "the cDNA contained in ATCC Deposit Number 979004" in claim 38, or an isolated antibody produced by immunizing an animal with a protein whose sequence comprises the amino acid sequence of the secreted polypeptide encoded by "the cDNA contained in ATCC Deposit Number 97904", wherein said antibody or protion thereof specifically binds to the polypeptide encoded by "the cDNA contained in ATCC Deposit Number 97904" in claim 52, or an isolated antibody or portion thereof that specifically binds to aprotein whose sequence consists of the amino acid sequence of the full-length polypeptide encoded by "the cDNA contained in ATCC Deposit Number 97904" in claim 61. The specification does not enable any person skilled in the art to which it pertains,

or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The terms "comprising" in claim 15 is open-ended, it expands the amino acid residues 25-123 fragment of SEQ ID NO: 200 to include additional non disclosed amino acids on either N-terminal, C-terminal or both terminals of amino acids 25-123 of SEQ ID NO: 200. It is recognized in the prior art that the function of a protein depends on the sequence of its amino acids in a certain pattern, conformation of the protein due to the amino acid sequence and the functional properties of the different parts of the protein. However, there does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make the various proteins recited in the instant claims. A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. Without detailed direction as to which amino acid sequences are essential to the function of the polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of protein sequences encompassed by the instant claims would share the function of the polypeptide of SEQ ID NO:200, other than the amino acid of SEQ ID NO:200.

Further, the ATCC deposit No. 97904 contains multiple different clones. It is recognized in the prior art that the multiple insertions in the same strain are only limited by the availability of distinct selection markers. Given the lack of marker specific for SEQ ID NO: 200, the claimed antibody is not specific for SEQ ID NO: 200 but the antibody would be raised against (bind to) multiple different proteins encoded by the multiple different cDNA contained in ATCC Deposit No. 97904. Further, the reproduction of the polypeptides from the disclosed deposit No. 97904 is an extremely unpredictable event because it is known that bacteria contain multiple different clones with the same antibiotic resistant would lead to selective pressure favoring some clones over others and there is no guarantee that the cDNA encoding the polypeptide of SEQ ID NO: 200 is going to be selected over time.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

11. Claims 1-74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of an antibody or portion thereof that specifically binds to a protein whose sequence consists of amino acid residues 25 to 123 of SEQ ID NO: 200, or an isolated antibody or portion thereof that specifically binds to a portion whose sequence consists of amino acid residues 1 to 123 of SEQ ID NO: 200.

Applicant is not in possession of any isolated antibody produce by immunizing an animal with any protein whose sequence "comprises" amino acid residues 25-123 of SEQ ID NO:200 in claim 15, or any isolated antibody or portion thereof that specifically binds to a protein whose sequence consists of the amino acid sequence of the secreted polypeptide encoded by "the cDNA contained in ATCC Deposit Number 979004" in claim 38, or an isolated antibody produced by immunizing an animal with a protein whose sequence comprises the amino acid sequence of the secreted polypeptide encoded by "the cDNA contained in ATCC Deposit Number 97904", wherein said antibody or protion thereof specifically binds to the polypeptide encoded by "the cDNA contained in ATCC Deposit Number 97904" in claim 52, or an isolated antibody or portion thereof that specifically binds to aprotein whose sequence consists of the amino acid sequence of the full-length polypeptide encoded by "the cDNA contained in ATCC Deposit Number 97904" in claim 61.

Applicant has disclosed only amino acid of SEQ ID NO: 200 and the amino acid 25-125 of SEQ ID NO: 200; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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March 5, 2004

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